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COLD PRESSOR TEST - A 20-YEAR FOLLOWUP STUDY OF 123 SUBJECTS

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FOREWORD

This report was prepared by the following personnel at the USAF School of Aerospace Medicine and the University of Washington—School of Medicine:

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ABSTRACT

In 1960 blood pressures were obtained on 106 active and retired military subjects on whom the cold pressor test had been performed in 1940. These blood pressures and the cold pressor index (rise in systolic blood pressure, millimeters of mercury) were analyzed for predictability of future hypertension from the index. The mean index of the 11 who became hypertensive was significantly larger than the mean index of the 51, of comparable age, 35 years and older, who remained normotensive. Statistical association was found between hyperreaction (using a cutting point of 10 mm. Hg) and hypertension; however, the accuracy of prediction is not good. Thus the test as defined is not recommended as a predictor of future hypertension.

An average increase in diastolic blood pressure of about 7 mm. Hg every 20 years was observed cross-sectionally in 1940 and longitudinally.

This technical documentary report has been reviewed and is approved.



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Chief, Operations Division

COLD PRESSOR TEST — A 20-YEAR FOLLOWUP STUDY OF 123 SUBJECTS

1. INTRODUCTION

In 1950, Armstrong and Rafferty (1) published a seven-year followup of Air Force officers on whom the cold pressor test was performed in 1940, according to the Hines and Brown technic (2). Since the test is still being appraised, a 20-year followup of available subjects from Armstrong's original group seemed appropriate.

Our data are pertinent to Hines's (3) statement that "the evidence is reasonably good that a person with vascular hyporeactivity will not have essential hypertension within 10 or 20 years. On the other hand, it is purely speculative whether a person who is a vascular hyperreactor will have essential hypertension later in life, although his chances seem considerably greater than those of the hyporeactor." But, he also wrote in the same paper: "The general use of the cold-pressor test to predict the future development of hypertension has not been advocated by me."

Hines and co-workers have used various criteria for a positive reaction to the cold pressor test. In 1940, the criteria for hyperreactors were a pressure rise of 21 mm. Hg systolic or 16 mm. Hg diastolic, or both (4). In 1951, the criterion was in terms of diastolic pressure rise alone: hyporeactors, 9 mm. Hg or less; normoreactors, 10 to 20 mm. Hg; and hyperreactors, 21 mm. Hg or more (3). In 1955, those subjects whose maximal diastolic blood pressures during the cold pressor test exceeded 84 mm. Hg were categorized as hyperreactors (5). Further, those whose maximal diastolic pressure did not exceed 84 mm. Hg were separated into two groups: those with rise in

pressure of less than 15 mm. Hg and those with rise of 15 mm. Hg or more. Although subjects with a reaction of less than 85 mm. Hg were separated into two groups, the groups were not thought to differ in proneness to develop hypertension.

For a review of cold pressor literature through 1950, the reader is referred to Wolff (6). More recent concepts concerning the role of increased cardiac output and the patterns of peripheral vasoconstriction in hypertensives and normotensives in cold pressor mechanisms are discussed by Boyer et al. (8) and Brod (9).

2. PROCEDURES

Cold pressor tests using Hines's technics were carried out on flying and nonflying officers at Wright Field in 1940. The cold pressor index employed was a rise in systolic blood pressure. No diastolic response to the test was recorded.

Owing to the difficulty of tracing people during World War II, it was arbitrarily decided that for this study, of the men tested in 1940 and reported on in 1947, only those listed in the 1947 military registers either in active duty or retired status, would be followed. The number of persons satisfying these criteria was 125. Two of these had severed their military connection between 1947 and 1950 and could not be located through military records. This left 123 subjects available for followup in 1960. Letters were sent to the living, requesting from them: three recent blood pressure readings, information concerning elevated blood pressures in the past, and antihypertensive medication, if any. For those who had died, records of the terminal hospitalization were

TABLE I
Number and percentage of subjects classified by 1940 systolic cold pressor index and by 1960 status*

Index (1940)	Number of subjects	Dead	Alive		
			Did not reply to questionnaire	Replied to questionnaire	
				Normotensive (1960)†	Hypertensive (1960)
1-9	61	7 (11.5)	3 (4.9)	49 (80.3)	2 (3.3)
10-14	36	1 (2.8)	1 (2.8)	29 (80.5)	5 (13.9)
15-20	21	2 (9.5)	2 (9.5)	15 (71.5)	2 (9.5)
21-30	5	1 (20.0)		2 (40.0)	2 (40.0)
Total	123	11 (8.9)	6 (4.9)	95 (77.3)	11 (8.9)

*Percentages are given in parentheses.

†Normotensive = 160/92 mm. Hg or less.

TABLE II
Means and ranges of 1940 systolic cold pressor index and diastolic blood pressure of subjects classified according to 1940 age and 1960 blood pressure status

Age (1940)	Normotensive (1960)*							Hypertensive (1960)†				
	Number of subjects	Index (1940)		Diastolic BP				Number of subjects	Index (1940)		Diastolic BP	
				1940		Difference 1960-1940					1940	
		Mean	Range	Mean	Range	Mean	Range		Mean	Range	Mean	Range
22-24	6	12.8	5-20	66.3	59-70	8.0	1 to 15					
25-29	13	9.8	5-22	68.6	62-78	6.9	-2 to 14					
30-34	25	9.9	2-18	70.5	56-84	8.2	-6 to 28					
35-39	30	10.2	1-22	70.7	58-89	9.0	-9 to 24	6	14.2	7-28	76.0	70-83
40-44	12	9.4	3-20	71.9	63-85	2.9	-24 to 17					
45-49	7	10.4	2-18	78.0	66-85	6.4	-3 to 22	3	16.0	6-30	79.0	76-81
50-54	2	4.0	2-6	77.0	72-82	9.0	-2 to 20	2	16.0	12-20	81.5	78-85

*Normotensive = 160/92 mm. Hg or less.

†Difference between the 1960 and 1940 blood pressure is not given since some of the 1960 hypertensives are on drugs.

TABLE III

Means of 1940 age and diastolic blood pressure of subjects classified according to 1940 systolic cold pressor index and 1960 blood pressure status

Index (1940)	Normotensive (1960)*				Hypertensive (1960)†		
	Number of subjects	1940 mean		Mean difference between 1960 and 1940 diastolic B.P.	Number of subjects	1940 mean	
		Age	Diastolic B.P.			Age	Diastolic B.P.
1-9	49	36.1	71.9	5.8	2	42.5	78.0
10-14	29	33.8	68.4	11.9	5	40.8	76.6
15-20	15	34.6	72.9	4.4	2	43.0	79.0
21-30	2	32.5	67.5	8.5	2	40.0	79.5
Total	96	35.1	70.9	7.5	11	41.4	77.8

*Normotensive = 150/92 mm. Hg or less.

†Difference between the 1960 and 1940 blood pressure is not given since some of the 1960 hypertensives are on drugs.

reviewed when available, and the death certificates were noted for any reference to hypertension and its related complications. Six of those reported as living, according to current retirement and active duty records, did not reply.

For purposes of this report, a mean blood pressure of 150/92 mm. Hg or less was considered to be normal. All of the 123 subjects had normal blood pressure readings in 1940. Their systolic cold pressor indexes ranged from 1 to 30.

3. RESULTS

Table I gives for the 123 subjects followed the number and percentage of the numbers in each 1940 systolic index group according to whether dead or living in 1960; if living and if they replied, whether normotensive or hypertensive. Among the 11 living hypertensives, 6 currently required antihypertensive medication. Of the remaining 5 subjects, 1 was being evaluated prior to therapy.

Two subjects (indexes of 3 and 10) were classified normotensive though 1 of 3 blood pressures was elevated. Only 5 subjects had an index of 21 or greater.

One of the 11 who died was hypertensive. His index was 16. Since those dying might not have lived long enough to develop hypertension, further discussion will be limited to those alive and followed for 20 years. A total of 106 subjects satisfied both of these criteria.

Table II presents data on these 106 subjects giving means and ranges of the 1940 index and diastolic blood pressure, and differences between 1960 and 1940 diastolic blood pressure of subjects within age and normotensive and hypertensive groups. All hypertensives in 1960 were 35 years or older in 1940. Within age groups, the hypertensives had slightly higher index means. Further, there is some indication that the diastolic pressure in 1940 of hypertensives was higher than that for normotensives of comparable age.

Table III presents data on the 106 subjects giving means and ranges of the 1940 age and diastolic blood pressure, and differences between 1960 and 1940 diastolic blood pressure, within index and normotensive and hypertensive groups. It should be noted that diastolic blood pressure and index value appear to be uncorrelated. Further, it should be observed that the mean age of hypertensives is 6.3 years greater than that of the normotensives.

4. DISCUSSION

Criteria for significance of reactivity have varied as data and experience have accumulated (2, 3, 4). Cold pressor indexes have been based on *change* in blood pressure as well as *level* of blood pressure. An index based on *level* of blood pressure attained would generally not give the same rank-ordering of subjects as an index based on *change*. Thus some subjects who would never be considered a hyperreactor under a *change* criterion would be considered a hyperreactor under a *level* criterion and vice versa. Such changes have been studied in normotensives and hypertensives.

The purpose of such a study as this one is to delineate in retrospect differences between those who developed hypertension and those who remained normotensive. In particular, it was to determine if an individual's response to cold, irrespective of the mechanism, did relate to his propensity to future hypertension.

A *change* index (difference between systolic pressure at rest and maximum systolic pressure during cold exposure) was employed in this study. Various cutoff points for the blood pressure change were used to define hyperreactors. Varying the cutoff point redefined hyperreactors, but left subjects in the same rank order. Unfortunately, the maximum diastolic pressures were not collected in 1940 on the subjects of this study so that none of the indexes based on maximum diastolic pressure can be checked for their predictability of hypertension.

Hines (4), in 1940, found an incidence of 15% hyperreactors in his population of normal subjects when he used the criteria of a 21 mm. Hg rise in systolic pressure or a 16 mm. Hg rise in diastolic pressure, or both. However, we observed only 4 hyperreactors out of 106 subjects when we used the criterion of a rise of 21 mm. Hg in systolic pressure.

For the subjects of this study, aged 22 to 54, there was no noticeable relationship between cold pressor index and age. The 1940 mean diastolic pressure of all subjects, normotensive

and hypertensive, of 35 years or older was significantly higher ($P < .01$) than that for subjects less than 35 years of age. A similar result was obtained for only the normotensives ($P < .05$).

The effect of aging on diastolic pressure can be seen, cross-sectionally, in table II: the older individuals had, on the average, a higher diastolic pressure than the younger men. From table III, we observed that, over time, or longitudinally, the average increase in diastolic pressure is 7.4 mm. Hg over the 20-year period. This increase is similar to that observed by Oldham et al. (7).

Since blood pressure increased with age and since all those who developed hypertension in 1960 were 35 years or older in 1940, only the 62 subjects 35 years and older were used for further comparison. The hypertensives had a mean cold pressor index of 15.0 mm. Hg (S.E., 2.41), which is significantly higher ($P < .05$) than the mean for normotensives of 9.8 (S.E., 0.69). The 1940 mean diastolic pressure of those developing hypertension was 77.8, significantly higher ($P < .05$) than the 1940 mean diastolic pressure of 72.2 for normotensives. For the normotensives, however, the 1960 diastolic and systolic pressures were not correlated with the cold pressor index.

With systolic increase of 21 mm. Hg or more used as the criterion for hyperreactivity, no significant association between test results and hypertension can be demonstrated. Nor can any strong association be demonstrated if one uses cutoffs of 17, 15, or 13 mm. Hg for hyperreactors. However, if the cutting point is dropped to 10, then at least for these data, there is a significant association between an index of 10 or more and the development of hypertension ($P < .05$).

Although a significant statistical difference was demonstrated between the mean index of those who became hypertensive and the mean index of those who remained normotensive, the association between the index and the development of hypertension is not of sufficient strength to recommend its use as a predictor of future hypertension.

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<p>USAF School of Aerospace Medicine, Brooks AF Base, Tex.</p> <p>SAM-TDR-62-137. COLD PRESSOR TEST—A 20-YEAR FOLLOWUP STUDY OF 123 SUBJECTS. Dec. 62, 5 pp. incl. tables, 9 refs.</p> <p>In 1960 blood pressures were obtained on 106 active and retired military subjects on whom the cold pressor test had been performed in 1940. These blood pressures and the cold pressor index (rise in systolic blood pressure, millimeters of mercury) were analyzed for predictability of future hypertension from the index. The mean index of the 11 who became hypertensive was significantly larger than the mean index of the 51, of comparable age,</p>		<p>USAF School of Aerospace Medicine, Brooks AF Base, Tex.</p> <p>SAM-TDR-62-137. COLD PRESSOR TEST—A 20-YEAR FOLLOWUP STUDY OF 123 SUBJECTS. Dec. 62, 5 pp. incl. tables, 9 refs.</p> <p>In 1960 blood pressures were obtained on 106 active and retired military subjects on whom the cold pressor test had been performed in 1940. These blood pressures and the cold pressor index (rise in systolic blood pressure, millimeters of mercury) were analyzed for predictability of future hypertension from the index. The mean index of the 11 who became hypertensive was significantly larger than the mean index of the 51, of comparable age,</p>	<p>1. Hypertension 2. Test, cold pressor 3. Aging effect on blood pressure</p> <p>I. AFSC Task No. 775501 II. Allen, M. F., Langdon, D. E. III. In ASTIA collection</p>
<p>USAF School of Aerospace Medicine, Brooks AF Base, Tex.</p> <p>SAM-TDR-62-137. COLD PRESSOR TEST—A 20-YEAR FOLLOWUP STUDY OF 123 SUBJECTS. Dec. 62, 5 pp. incl. tables, 9 refs.</p> <p>In 1960 blood pressures were obtained on 106 active and retired military subjects on whom the cold pressor test had been performed in 1940. These blood pressures and the cold pressor index (rise in systolic blood pressure, millimeters of mercury) were analyzed for predictability of future hypertension from the index. The mean index of the 11 who became hypertensive was significantly larger than the mean index of the 51, of comparable age,</p>		<p>USAF School of Aerospace Medicine, Brooks AF Base, Tex.</p> <p>SAM-TDR-62-137. COLD PRESSOR TEST—A 20-YEAR FOLLOWUP STUDY OF 123 SUBJECTS. Dec. 62, 5 pp. incl. tables, 9 refs.</p> <p>In 1960 blood pressures were obtained on 106 active and retired military subjects on whom the cold pressor test had been performed in 1940. These blood pressures and the cold pressor index (rise in systolic blood pressure, millimeters of mercury) were analyzed for predictability of future hypertension from the index. The mean index of the 11 who became hypertensive was significantly larger than the mean index of the 51, of comparable age,</p>	<p>1. Hypertension 2. Test, cold pressor 3. Aging effect on blood pressure</p> <p>I. AFSC Task No. 775501 II. Allen, M. F., Langdon, D. E. III. In ASTIA collection</p>

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